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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,548	01/15/2002	Randall W. Nelson	530-011A	5003

7590 05/27/2005

The Halvorson Law Firm
Ste 1
405 W. Southern Ave.
Tempe, AZ 85282

EXAMINER	
SAKELARIS, SALLY A	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,548	NELSON ET AL.	
	Examiner	Art Unit	
	Sally A. Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☒ Claim(s) *4 and 7-12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-6-0-

DETAILED ACTION

This action is written in response to applicant's correspondence submitted 3/14/2005. Claims 1, 4, 5, and 7-10 have been amended, no claims have been canceled, and claims 11 and 12 have been added. Claims 1-12 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Specification

The amendment filed 3/14/2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Page 7 of the specification. While applicant argued on page 2 of their 8/23/2004 submission that the page was "inadvertently excluded at the time the application was filed" specific omissions were made at the time of filing as a result of the omission of page 7 of the specification. Furthermore, applicant asserts on page 1 of their 3/14/2005 submission that "support for the information contained on missing page 7 can be found throughout the entirety of the application". However, applicant has not specifically disclosed where in the specification this support exists (e.g. for "a stationary robot head composed of multiple positions for chemical modification, microcolumn functionalization, biofluids analysis", etc.)

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim objections

1. Claims 4 and 7-10 and new claims 11 and 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 4, 7-9, and 10-12 are objected to as these claims are drawn to only to an intended use of the present invention.

Applicant should note that the following art rejection is made in light of the claim objections above. Claims 4 and 7-12 below, have been rejected in view of their lacking patentable limitations required when claiming an apparatus such as their high throughput integrated system. Even if applicant amends their claims to include language that distinguishes it from the prior art in terms of structure rather than function and further any claims recitation of an intended use, an art rejection has been supplied to illustrate the obviousness that exists in the prior art even if these objections are remedied.

Response to Arguments

Applicant's arguments filed 3/14/2005 have been fully considered but they are not persuasive. While applicants assert that they have amended claims 4, 5, and 7-10 to place the claims in proper dependent form on page 5 of their response, only claim 5 appears to have been properly amended. Claims 4, 7-10 and new claims 11-12 contain limitations only to an intended use of the present invention or components thereof. Applicant's recitations of "for retrieving

biological molecules", "capable of being rinsed free of non-specifically retained compounds", "for depositing selectively retained biological molecules", "means for the robotic...", "a robotic to lower", and finally "comprising a robot to rinse" are not viewed as providing any structural limitation to the claims, merely intended uses of the invention. Appropriate correction is recommended.

THE FOLLOWING ARE NEW REJECTIONS NECESSITATED BY APPLICANT'S AMENDMENTS TO THE CLAIMS

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 5 is indefinite over the recitation of "modifying agent". This phrase makes the claims unclear because the specification does not define what is encompassed by a "modifying agent". There is no fixed definition in the art for what constitutes a modifying agent in the context of mass spectrometer targets. It is unclear, eg. whether the term refers to a variant or modification of the size and/or nature of the analytes or instead a modification of the matrix material(i.e., application method differs of matrix such as through a pipette, delivery through piezoelectric "ink" jets, or painting using a mechanical applicator). It is suggested that the claims be amended to clarify what is being modified and how the modifying agent is changing the mass spectrometer target.

Claim Rejections - 35 USC § 103

The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114).

The courts have further stated that a claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. Ex parte Masham, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson et al.(US Patent 6,569,383) in view of Wagner et al.(US Patent 6,329,209B1).

With regard to claim 1, Nelson et al. teach a high throughput integrated system for qualitative and quantitative biomolecules analysis comprising;

a) a robotic platform, taught in the reference as a bioactive chip(BC) fitted with multiple, spatially arrayed affinity capture mechanisms located at separation sites(for ex. Clm 1) where the separation site, SS, can "accomplish isolation, or separation, of the target analyte, particularly by methods such as affinity capture" and that may be "accomplished using multiple separation sites SS, either in series or in parallel"(Col. 12 lines 26-33).

b) a mass spectrometer target, different and separate from the spatially arrayed affinity microcolumns(see FIG.1 and the analytes of the PS that are different and separate from the microcolumns of the SS and MS sites also see Col. 15 lines 48-50 regarding alternative sampling techniques)and having a spatial array corresponding to the same spatial array as the affinity captures at the SS as the reference teaches "depending upon the size and nature of the analyte captured by the bioactive chip BC, matrix material may optionally be employed"(Col. 15-16) and "with regard to MALDI, laser energy is impinged upon the surface of the bioactive chip BC, resulting in the desorption/ionization of the captured analyte"(Col. 16 lines 60-63) and "the ionized analyte is then detected by the mass spectrometer"(Col. 16 lines 63-64).

c) a mass spectrometer capable of accepting the spatially arrayed target as the reference teaches that "the laser is directed to the surface of the bioactive chip BC having the analyte captured thereon"(Col. 16 lines 64-65) and "when multiple active sites, SS-PS-MS, are employed on a single bioactive chip BC, the laser may be directed to a single active site at a

time...in this manner, the captured analyte from the single may be analyzed by mass spectrometry"(Col. 17 lines 4-10).

With regard to claim 2, the reference teaches that multiple active sites are included in the invention as Figure 1 exemplifies in its rendering of the surface of the Bioactive chip, BC that sports 7 separation sites, 5 processing sites, and 8 modifying sites, which amount to 20 elements that anticipate the spatial array comprising between 4 and 1536 elements.

With regard to claim 3, the reference teaches the above system wherein the platform comprises multiple processing stages in their teaching of the BC with "separate addressable sites, for the purposes of analyte separation, processing and modification is used in conjunction with a microfluidics system capable of precise delivery, in terms of location, time and volume, of analyte to each of the addressable sites present on the chip"(Col. 4 lines 50-54, see also claims 1 and 21).

With regard to claims 4, 7, and 10 the reference teaches that "the surface immobilized affinants of the at least one separation site are able to isolate the analyte from the complex solution"(Clm 5) and further that wherein the separating molecules isolate the analyte by affinity capture(Clm 6), and lastly Example 1 teaches the specificity of the separation site in its MALDI-TOF interrogation of IL-1α and lacking signals for Has and the antibody(Col. 17 lines 42-66), which all anticipate the limitation of the affinity capture, SS, receiving specific biological molecules in a biological media, the specific biological molecules are retrieved via affinity interaction. As a result the reference teaches the system of claim 1 wherein the spatially arrayed affinity microcolumns comprise an affinity reagent for retrieving biological molecules contained in a biological media.

With regard to claim 5, the reference teaches that the mass spectrometer target does have modifying activities and modifying agents such as in claims 2-4 where the reference teaches that the "surface immobilized modifiers of the at least one modification site modify the analyte by digesting or processing the separated analyte in to modified fragments" and further that the modifying molecules(aka agents) have an enzymatic activity or are proteins.(Col. 25)

With regard to claim 6, the reference teaches that the mass spectrometer is a matrix-assisted laser desorption/ionization time-of-flight mass spectrometer(For ex. Ex. 1, Col. 3, Col. 5 lines 5-8, etc.).

With regard to claim 8, the reference teaches the bioactive chip wherein one of the multiple processing stages comprises affinity microcolumns capable of being rinsed free of non-specifically retained compounds in their teaching in Col. 5 lines 25-28 of "washing unwanted biomolecules from the surroundings of the captured analyte; transferring the captured analyte from the separation site to a modifying site"(Nelson et al.)

With regard to claim 9, the reference teaches this system wherein at least one of the multiple processing stages comprises a mass spectrometer target for depositing selectively retained biological molecules in Col. 17 as "critical to the success of the BCMS(bioactive chip mass spectrometry) are the following: the ability to perform different operations(affinity capture, post separation processing, or enzymatic treatment) on different action sites on the bioactive chip BC, and spatially resolve the different actions sites throughout the entire process; the use of IA and MS(preferably MALDI-TOF) to analyze multi-component affinity systems; achieving high specificity and sensitivity analyses when targeting analytes present in complex mixtures"(Col. 17 lines 20-33).

Nelson et al. do not teach the above system of claims 1-10 and new claims 11 and 12 wherein the affinity capture component is in the form of an affinity microcolumn or comprises a robotic pipette delivery system.

However, Wagner et al. teach arrays of protein-capture agents and methods of use thereof. Wagner et al. teach that to avoid "protein capture agents that recognize common proteins or proteins of non-interest" the library is passed "over an affinity surface, such as a chromatography column, containing cross-linked proteins of non-interest". "The 'flowthrough' containing capture agents that did not react with the affinity surface is collected"(col. 29 lines 12-17) after passage through the affinity column. Furthermore, with regard to new claims 11 and 12, Wagner et al teach Hamilton 2200 robotic pipetting delivery system for use in the parallel processing of samples(DETX 115).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the specific type of arrayed microcolumns and robotic pipetting delivery system taught by Wagner et al. in view of the array-based affinity capture mechanism taught by Nelson et al. since "maintaining protein activity at the liquid-solid interface requires entirely different immobilization strategies than those for nucleic acids and that the proper orientation of the antibody or other protein at the interface is desirable to ensure accessibility of their active sites with interacting molecules"(Wagner et al. Col. 2 lines 40-47) as taught by Wagner's column-shaped capture mechanisms, is the expected benefit of conferring this more specific affinity reaction in a peptide array.

Response to Arguments

Applicant's arguments filed 3/14/2005 have been fully considered but they are not persuasive. Applicant's arguments with respect to claims 1-10 have been considered but are moot in view of the new ground(s) of rejection and in further view of the claims limited to intended uses only. Applicant is reminded that their claims must recite structural limitations, not merely intended uses in order to overcome the cited prior art.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Related Cited Art

1. Mansfield et al. US Patent 6,156,178

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A. Sakelaris whose telephone number is 571-272-0748. The examiner can normally be reached on M-Fri, 9-6:30 1st Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

5/24/2004

Sally Sakelaris

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600